

Incidence of Tuberculosis Disease among Household Contacts of Adult Pulmonary Tuberculosis Patients in India-CTRIUMPH A Multi Centric Cohort Study

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Background

- WHO's new End TB Strategy 2035
 - 90% reduction in TB incidence
 - 95% reduction in TB deaths
- Preventing development of active TB
 - Break the cycle of transmission
 - Decrease the overall burden of TB worldwide [JuanPabloMillet 2013]
- Household Contacts (HHC) of Pulmonary TB (PTB) patients
 - High risk for developing TB disease [WHO 2012,RNTCP TOG2016]
 - High quality estimates of TB incidence are needed for TB vaccine trials focused on prevention of disease (POD)
- India has 27% of world's TB burden and therefore an important place to estimate incidence

Objective

- *Primary Objective:* To estimate the incidence of TB disease among household contacts of newly diagnosed adult PTB patients started on TB treatment in India
- *Secondary Objective:* To determine the factors associated with incidence of TB disease among these household contacts

Methods

- **Study Design:** Multi centric Cohort Study
(CTRIUMPH *Gupte et al BMJ Open 2016*)
- **Study Settings:** Chennai [NIRT] and Pune [BJMC]
- **Study Period:** March 2014- December 2017
 - Recruitment completed and follow up ongoing
- **Active TB Cohort (Cohort A):** Adults with newly diagnosed PTB starting RNTCP Category I treatment [2EHRZ3/4RH3]
- **Household Contact cohort (Cohort B):** defined to include all adults and children living in the same house as the adult (18+yrs) PTB participant during the 3 months prior to diagnosis of TB
 - followed for 24 months and assessed for TB at baseline, 4-6 months, 12, 18 and 24 months

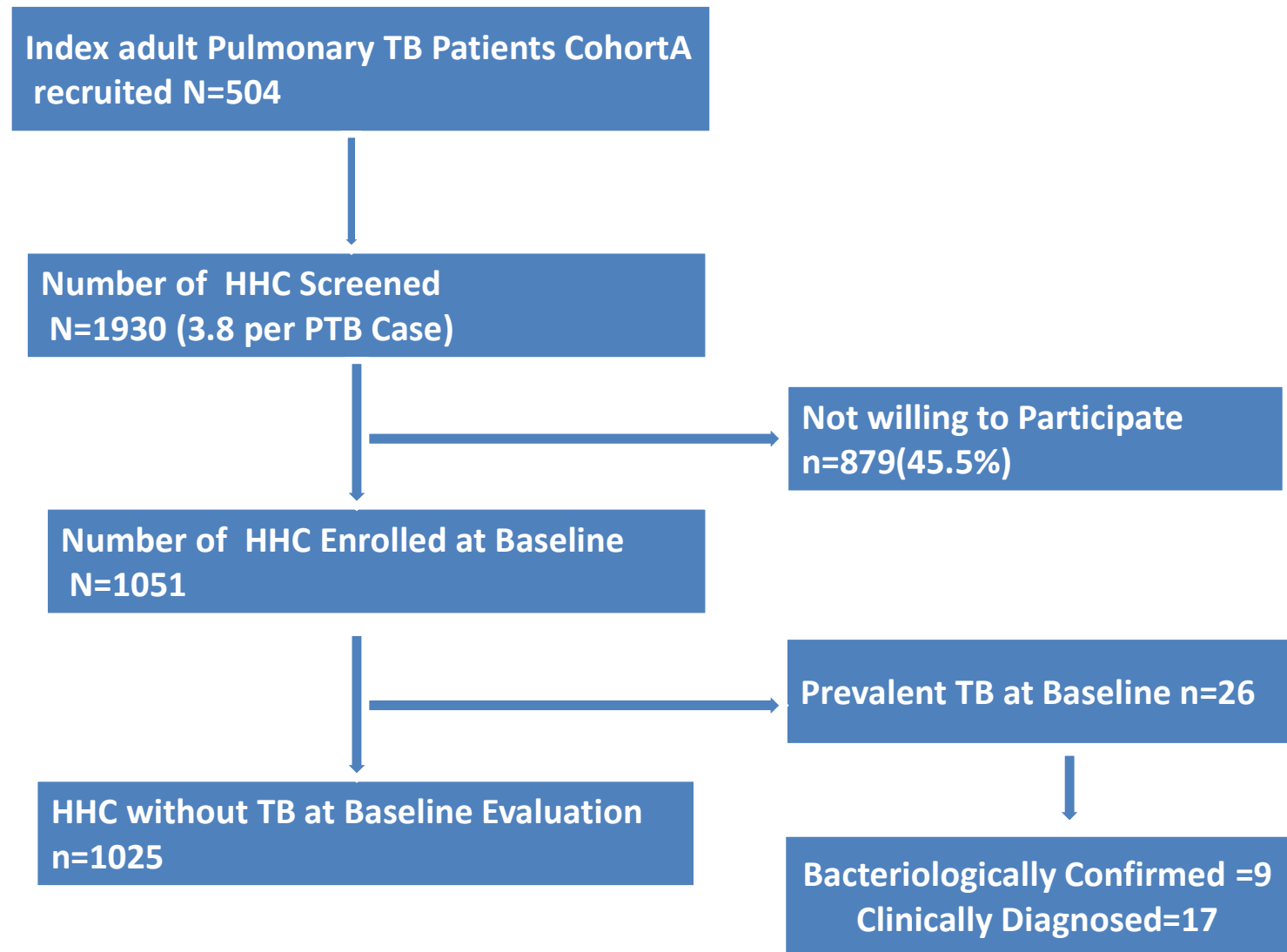
Outcome

- Incident TB defined as occurrence of *TB disease >1month to 24 months*
- Prevalent TB defined as occurrence of *TB disease within 1 month* of initial household screening
- A case of TB disease diagnosed on the basis of any of the following:
 - Microbiologically confirmed [smear, CBNAAT, culture]
 - Clinically diagnosed [X-ray abnormalities, histopathology and/or clinical signs suggestive of TB]
- TB infection positive defined as any HHC positive by TST >5mm and/or QuantiFERON Gold In Tube test (QGIT) ≥ 0.35 IU/mL.

Data Collection and Analysis

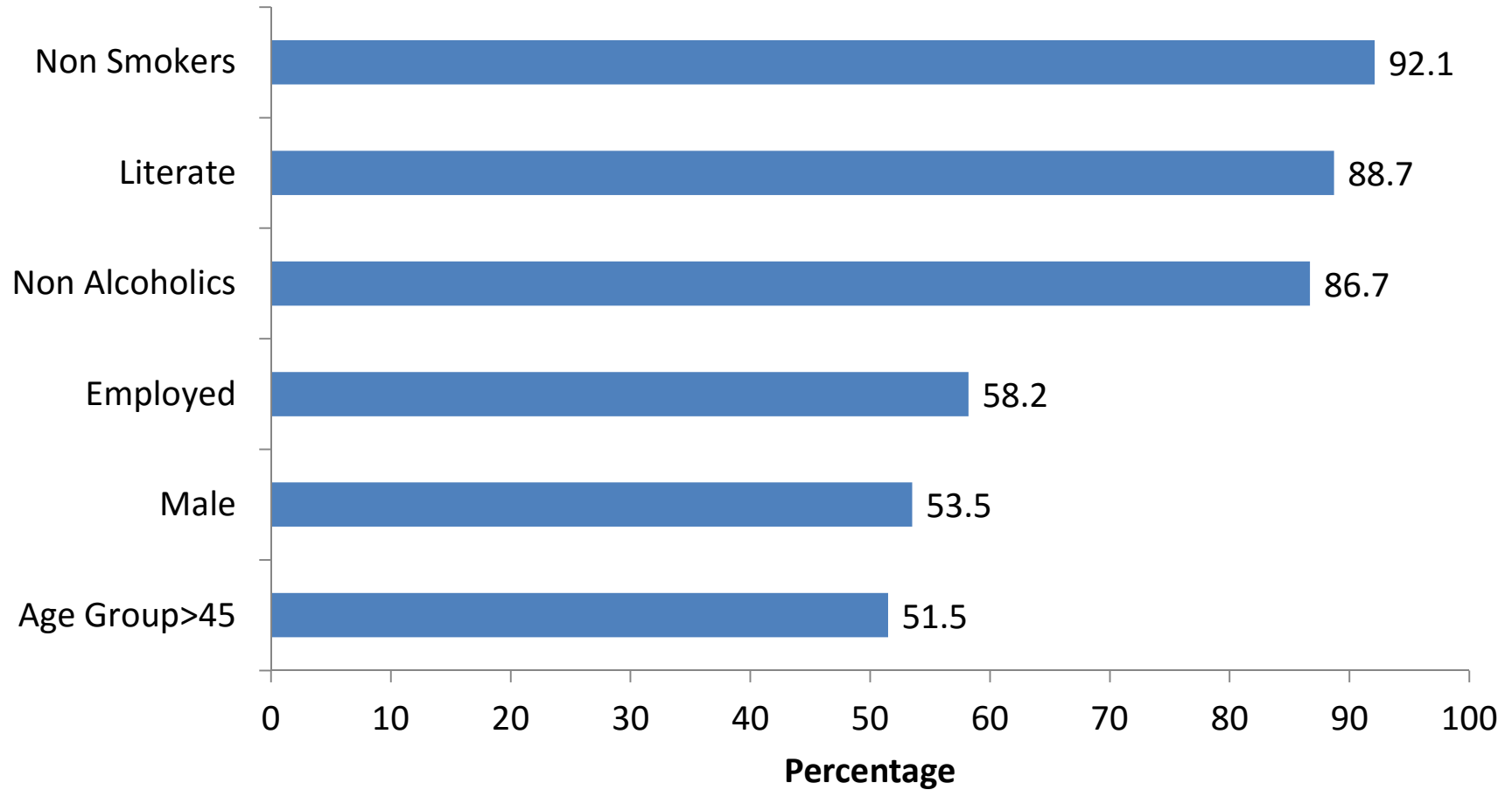
- Institutional Ethics Committee Approvals at NIRT, BJGMC, JHU
- Trained study staff collected data
 - Pre-tested questionnaire after written Informed Consent
- Data analyzed using STATA 15
- *Interim analysis*
- Incident rate ratios and 95% CIs
- Kaplan-Meier curves for occurrence of TB disease
- Adjusted Relative Risk (aRR) for TB incidence
 - Poisson regression adjusted for the household clustering and factors significant at 20% level by univariate analysis

Study Screening and Recruitment

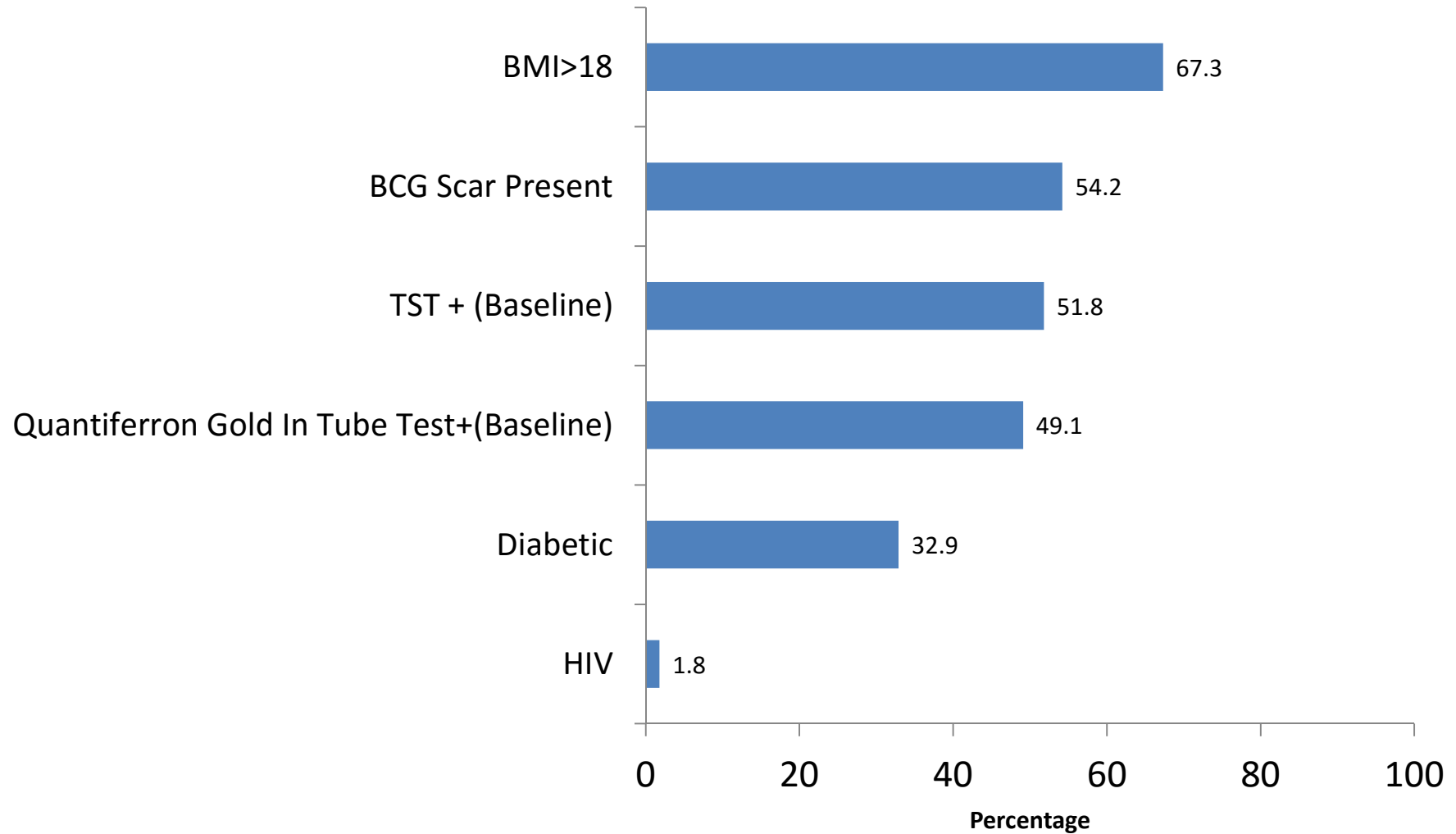


Out of 1025, 839 had completed a minimum of 12 Months of Follow-up

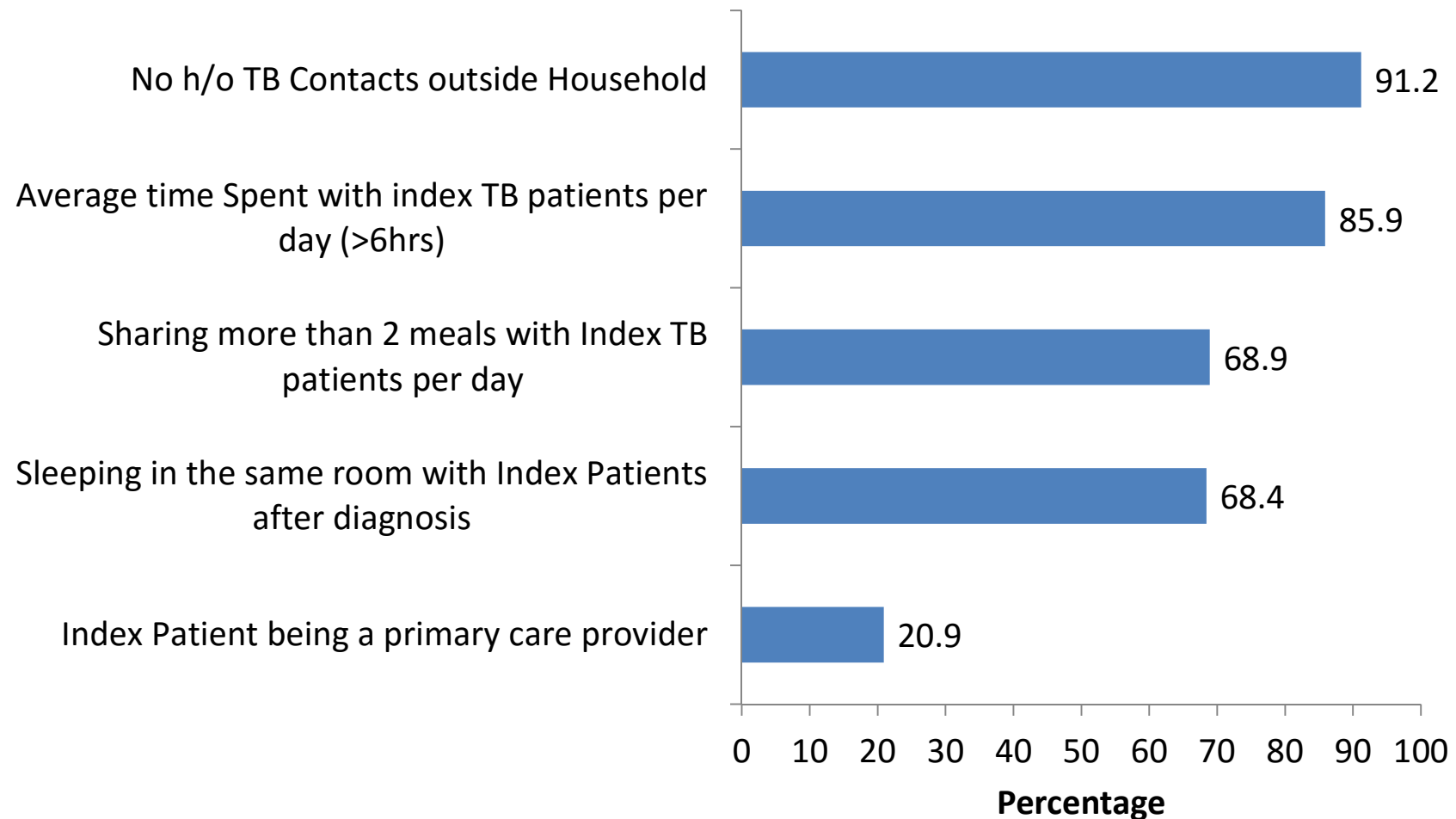
HHC-Demographic Characteristics [N=839]



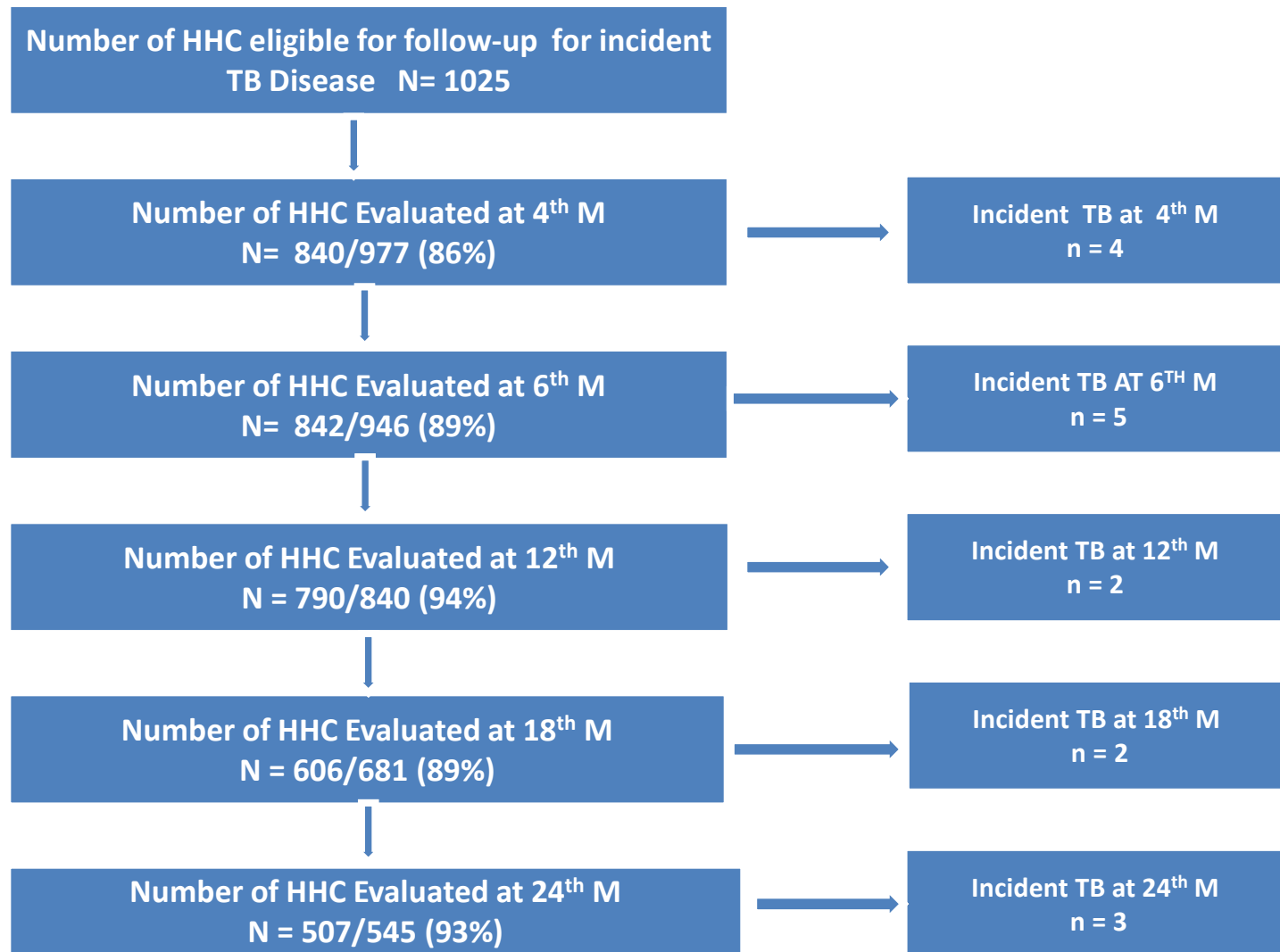
HHC- Clinical Characteristics [N=839]



HHC -Behavioural Characteristics[N=839]



Study Follow-up



Incident TB Cases =16
Bacteriologically Confirmed =5 **Clinically Diagnosed=11**
Pulmonary TB=13 **Extra Pulmonary TB=3**

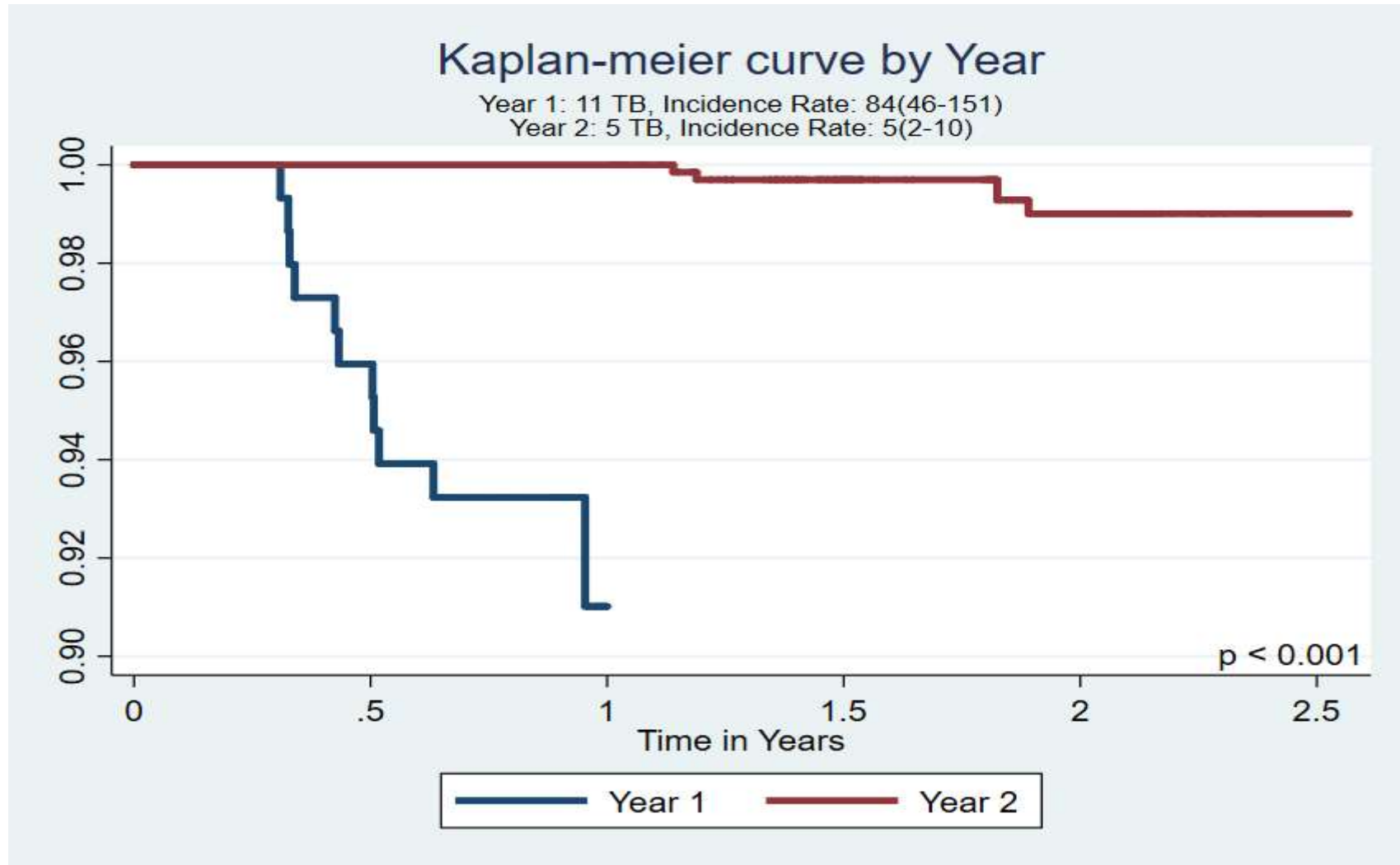
Incidence Rate Ratio of TB by age and gender

Characteristics	N	Number of TB cases	Person-Years of Follow-up	Rate (95% CI)/1000 PYF	
Age Group	< 6	68	1	106	9.4 (1.32 - 66.71)
	6-14	156	6	255	23.53 (10.57 - 52.37)
	14-25	183	2	310	6.46 (1.61 - 25.82)
	> 25	432	7	714	9.81 (4.67 - 20.57)
Gender	Male	392	10	731	15.29 (8.23 - 28.42)
	Female	447	6	654	8.21 (3.69 - 18.27)
Total	839	16	1385	11.55 (7.08 - 18.86)	

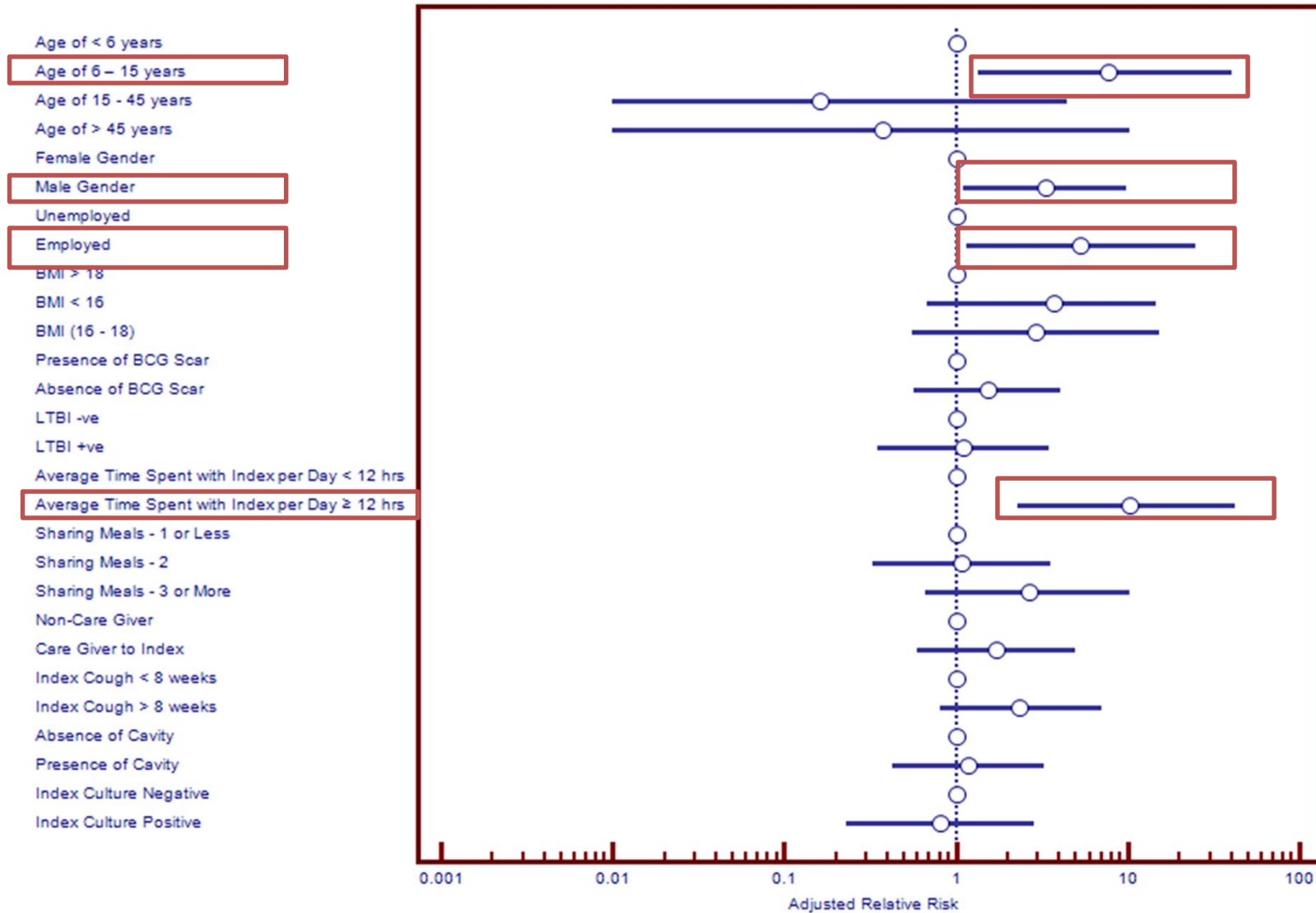
Incidence Rate Ratio of TB by Infection Status

Test		N	Number of TB cases	Person-Years of Follow-Up (PYF)	Rate (95% CI)/1000 PYF
TST (5 mm)	Pos.	435	7	727	9.64 (4.6 - 20.22)
	Neg.	377	6	618	9.71 (4.36 - 21.61)
Quantiferon Gold in Tube Test	Pos.	412	9	698	12.9 (6.71 - 24.8)
	Neg.	346	6	569	10.53 (4.73 - 23.45)
TST (5 mm) & Quantiferon Gold in Tube Test	T+ Q+	252	5	425	11.77 (4.9 - 28.28)
	T+ Q-	148	2	248	8.05 (2.01 - 32.21)
	T- Q+	148	2	256	7.83 (1.96 - 31.3)
	T- Q-	190	4	306	13.06 (4.9 - 34.8)

Timing of TB Disease Incidence



Factors associated with development of Incident TB in HHC of PTB patients



Comparison with Systematic Review and Meta-analysis on Contact investigation for TB

Measure		Fox, Gregory J., et al. % (95% CI)	Our Study % (95% CI)
Incident TB disease	Year 1	1.6 (0.8–3.3)	1.4 (0.7-2.3)
	Year 2	0.4 (0.2–0.9)	0.6 (0.3-1.4)
Co-Prevalent TB Disease		4.1 (2.6–6.4)	2.5 (1.7-3.6)

Recommendations for investigating contacts of persons with infectious tuberculosis in low- and middle-income countries.WHO.2012

Fox, Gregory J., et al. "Contact investigation for tuberculosis: a systematic review and meta-analysis." European Respiratory Journal 41.1 (2013): 140-156.

Conclusion

- Majority of Incident TB disease among HHC
 - Occurs within the first 12 months of index TB patient diagnosis
- Higher Risk for TB disease Incidence among HHC of PTB
 - Age group between 6-15 years
 - Male Gender
 - Employed
 - Increased exposure to Index patient per Day
 - Longer Index Patient Cough Duration

Recommendation

- Systematic implementation of Contact Screening
 - All age groups of the HHC of PTB patients
 - Close follow up for TB disease break down
- Inclusion of 6-15 years age group for chemoprophylaxis
- Health Education
 - Cough Hygiene for index TB patients
 - To increase awareness about TB symptoms
 - For early diagnosis of TB cases to prevent transmission

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Thank you